UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/686,880	10/12/2000	Austin G. Smith	06999.0009	5994

22852 7590 12/12/2002

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
1300 I STREET, NW
WASHINGTON, DC 20006

EXAMINER	
CHEN, SHIN LIN	
ART UNIT	PAPER NUMBER
1632	19

DATE MAILED: 12/12/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/686,880	Smith et al.
Examiner	**Art Unit**
Shin-Lin Chen	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Oct 7, 2002*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *42, 44-51, 53, 54, 58, 64, and 65* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *42, 44-51, 53, 54, 58, 64, and 65* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Applicants' amendment filed 10-7-02 has been entered. Claims 43, 52, 55-57 and 59-63 have been canceled. Claims 42, 44-49 and 53 have been amended. Claims 42, 44-51, 53, 54, 58, 64 and 65 are pending and under consideration.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 42, 44-51, 53, 54, 58, 64 and 65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "pluripotential cell" in claims 42 and 44-49 is vague and renders the claims indefinite. It is unclear as to the metes and bounds of what would be considered "pluripotential cell". The definition published by National Institutes of Health (Stem cells: A Primer, http://www.nih.gov/news/stemcell/primer.htm, May 2000, p. 1-6) indicates that the fertilized egg is totipotent, the inner cell mass cells, where embryonic stem cells are derived, are **pluripotent**, and the more specialized stem cells are multipotent. Embryonic stem (ES) cells and embryonic germ (EG) cells are considered pluripotent cells. Therefore, ES and EG cells are not **pluripotential** cells. Changing "pluripotential cell" ro "pluripotent cell" would be remedial. Claims 50, 51, 53, 54, 58, 64 and 65 depend on claim 42 but fail to clarify the indefiniteness.

The phrase "genetically modifying pluripotential cells to delete, mutate, substitute or add genes" in claim 45 is vague and renders the claim indefinite. It is unclear how a pluripotential cell can delete, mutate, substitute or add genes. It is also unclear what genes are intended and where those genes are introduced into, the pluripotential cells or neural progenitor cells. The phrase "neural progenitor" in claim 45 is vague and renders the claim indefinite. It is unclear as to the metes and bounds of what would be considered "neural progenitor". It is unclear whether a neural progenitor cell or a neural progenitor specific gene or other is intended.

The term "and/or" in claim 45 is vague and renders the claim indefinite. It is unclear what is intended to be claimed. Changing the term "and/or" to "...or...or both" would be remedial.

The phrase "the method comprises forming an embryoid body" in claim 49 is vague and renders the claim indefinite. It is unclear at what stage of the method the embryoid body is formed. Claims 50 and 51 depend on claim 49 but fail to clarify the indefiniteness.

The phrase "neural progenitors" in claim 65 is vague and renders the claim indefinite. It is unclear as to the metes and bounds of what would be considered "neural progenitors". It is unclear whether a neural progenitor cell or a neural progenitor specific gene or other is intended.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 42, 44-51, 53, 54, 58, 64 and 65 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for generating a neural progenitor cell culture by integrating selectable marker gene, such as neo, into Sox 2 gene that is induced by retinoic acid and said marker gene is under the control of Sox 2 gene promoter, does not reasonably provide enablement for a method for generating a neural progenitor cell culture by introducing into a pluripotent cell a selectable marker and/or a second selectable marker that is differentially expressed in neural progenitor cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 42, 44-51, 53, 54, 58, 64 and 65 are directed to a method for generating a neural progenitor cell culture from pluripotential cells, such as ES, EG or EC cells, by introducing into the pluripotent cell a selectable marker and/or a second selectable marker that is differentially expressed in neural progenitor cells, or using a selectable marker that is expressed in cells that express a Sox gene including Sox 1, Sox 2 and Sox 3 genes, a method of preparing a neural progenitor cell for storage, and a method of generating purified neurons by using the method set forth above.

The claims encompass using any selectable marker that is differentially expressed in neural progenitor cells, or using selectable marker that is expressed in cells that express a Sox gene. The specification discloses generating a neural progenitor cell culture by inducing ES cells

differentiation with retinoid acid and integrating selectable marker gene, such as neo, into Sox 2 gene of said pluripotent cells for selection of neural progenitor cells, wherein said marker gene is under the control of Sox 2 gene promoter.

The specification fails to provide adequate guidance and evidence that mere introduction of one or two selectable marker into any pluripotent cells and/or using cells expressing gene other than Sox 2 gene would produce purified neural progenitor cells. The selectable marker has to be integrated into a gene and under the control of the promoter of said gene, or promoter that is specific for neural progenitor cells, that is expressed during the differentiation of the pluripotent cells to neural progenitor cells because the selectable marker needs to be expressed during the process of differentiating into neural progenitor cells in order to select neural progenitor cells. A neural specific marker gene itself expressed inside the pluripotent cells may be used as a marker for identifying neural progenitor cells but it is insufficient for producing purified and enriched neural progenitor cells because non-neural progenitor cells need to be removed by selection pressure, such as antibiotics. There is no evidence of record that mere introduction of one or two selectable marker into any pluripotent cells, either via random integration or homologous recombination, and/or using cells expressing gene other than Sox 2 gene would produce purified neural progenitor cells. The purification and enrichment of neural progenitor cells during the differentiation of any pluripotent cells to neural progenitor cells require selection pressure that can remove non-neural progenitor cells and such selection pressure needs to be in a neural progenitor cell specific manner. In view of the reasons set forth above,

one skilled in the art at the time of the invention would not know how to use the claimed invention and would require undue experimentation to practice over the full scope of the invention claimed.

The specification also fails to provide adequate guidance and evidence of using stimulant other than retinoic acid to stimulate differentiation of any pluripotent cells to neural progenitor cells and using cells expressing gene other than Sox genes for producing neural progenitor cells. Different stimulant could stimulate different set of gene expression in pluripotent cells and the specification fails to disclose what genes would be expressed by stimulant other than retinoic acid during the differentiation of any pluripotent cells to neural progenitor cells. Absent the revelation of the genes that would be induced during the differentiation of any pluripotent cells to neural progenitor cells by stimulant other than retinoic acid, one skilled in the art at the time of the invention would not know how to use the claimed invention. In addition, the specification fails to provide adequate guidance and evidence that those gene expression during differentiation of any pluripotent cells to neural progenitor cells would be sufficient for the selection and enrichment of the neural progenitor cells against non-neural progenitor cells. In view of such, one skilled in the art at the time of the invention would require undue experimentation to practice over the full scope of the invention claimed.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. The examiner can normally be reached on Monday to Friday from 9 am to 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on (703) 305-4051. The fax phone number for this group is (703) 308-4242.

Questions of formal matters can be directed to the patent analyst, Patsy Zimmerman, whose telephone number is (703) 305-2758.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.